Clinical Policy: Prademagene Zamikeracel (Zevaskyn)

Reference Number: CP.PHAR.609
Effective Date: 04.29.25
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Prademagene zamikeracel (Zevaskyn™) is an autologous cell sheet-based gene therapy.

FDA Approved Indication(s)

Zevaskyn is indicated for the treatment of wounds in adults and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

All requests reviewed under this policy **require Precision Drug Action Committee (PDAC) Utilization Management Review**. Refer to CC.PHAR.21 for process details.

It is the policy of health plans affiliated with Centene Corporation® that Zevaskyn is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Recessive Dystrophic Epidermolysis Bullosa (must meet all)**:**

1. Diagnosis of RDEB as evidenced by two copies of positive collagen type VII alpha 1 chain (COL7A1) gene mutation confirmed by genetic testing (*see Appendix E*);
2. Prescribed by or in consultation with a geneticist, dermatologist, or histopathologist;
3. Age ≥ 6 years;
4. Provider attestation that member is concomitantly receiving standard of care preventative or treatment therapies for wound care (e.g., polymeric membrane, super-absorbent dressings, soft-silicone foam, enzyme alginogel, protease; *see Appendix F)*;
5. Wound sites meet all of the following (a, b, c, and d; *see Appendix D*):
   a. Chronic and open (e.g., stage 2 chronic wound);
   b. Area of at least 20 cm^2;
   c. Present for at least 6 months;
   d. Have not previously been treated with Zevaskyn;
6. Member does not have current evidence or history of squamous cell carcinoma in the area that will undergo treatment;
7. Zevaskyn is not prescribed concurrently with Vyjuvek™ or Filsuvez®;
8. Dose does not exceed 12 sheets per one-time surgical application.

Approval duration: 3 months *(1 surgical application)*

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Recessive Dystrophic Epidermolysis Bullosa
1. Re-authorization is not permitted. Members must meet the initial approval criteria if request is for previously untreated or newly developed wounds.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DEB: dystrophic epidermolysis bullosa
EB: epidermolysis bullosa
FDA: Food and Drug Administration
RDEB: recessive dystrophic epidermolysis bullosa

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- RDEB is an ultra-rare epidermolysis bullosa (EB) subtype caused by mutations in the COL7A1 gene.
- Inherited EB has four main classifications relating to the affected layer of skin: EB simplex, junctional EB, dystrophic EB, and Kindler's EB.
- Wound staging:
  - Stage 1: Unbroken skin
  - Stage 2: Partial-thickness skin loss with exposed dermis
  - Stage 3: Full-thickness skin loss with exposed adipose
  - Stage 4: Full-thickness skin loss and tissue loss

Appendix E: Diagnosis Information

- Per 2020 Clinical Practice Guidelines for Laboratory Diagnosis of EB, genetic testing is always recommended for the diagnosis of EB.
- Per 2017 Best Practice Guidelines for Skin and Wound Care in EB, definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence, antigenic mapping, and TEM.

Appendix F: Recommended Wound Care for DEB

- Wounds should be dressed with nonadherent silicone dressings, foam dressings that absorb exudates, and nonadherent silicone-based tape. Diluted bleach baths or compresses, topical antiseptics, and topic antibiotics are used as preventative measures against bacterial infections.
- Standard of Care for wound care per 2017 Best Practice Guidelines for skin and wound care in EB:
  - First choice of dressing when available:
    - Chronic or acute wounds – PolyMem
    - Super-absorbent – Cutimed Siltec
- Recommended dressings for DEB per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
Polymeric membrane	PolyMem	• Where cleansing is required • Chronic wounds	• Stimulates high levels of exudate • Distinct smell does not necessarily indicate infection • Can still be difficult to retain on vertical surfaces	• Change frequently until exudate reduces
Super-absorbent dressings	• Cutimed Siltec • Sorbion Sachet S • Filvasorb/ Vilwasorb Pro • Kerramax Care	• High exudate levels	• Can be cut between super-absorbent crystals, which appear in rows (as opposed to cutting across the crystal lattice)	
Soft silicone mesh	• Mepitel • Mepitel One • Adaptic Touch • Cuticell Contact	• Moist wound • Contact layer		
Lipido-colloid	• Urgo Tul	• Moist wound, drier wounds, and protection of vulnerable healed areas • Used as an alternative to soft silicon (see above) in the presence of over-granulation	• Where retention is difficult (e.g., vertical surfaces)	
Soft silicone foam	• Mepilex • Mepilex Lite • Mepilex Transfer	• Absorption of exudate • Protection • Lightly exuding wounds • To transfer exudate to absorbent dressing	• Over-heating • May need to apply over recommended atraumatic primary dressing	

Dressing Type	Brand	Indication/ Function	Contraindication/ Comments	Wear Time
		• Where conformability is required (e.g., digits, axillae)		
Foam	• Allevyn • UrgoTul Absorb • Aquacel Foam	• Absorption and protection	• May adhere if placed directly on wound bed, use alternative contact layer	
Bordered foam dressings	• Mepilex Border/ Mepliex Border Lite • Biatain Silicone Border/ Biatain Border Lite • Allevyn Gentle Border • Allevyn Border Lite • Kerrafoam • UrgoTul Absorb Border	• Isolated wounds • DDEB and mild RDEB	• Bordered dressings may require removal with SMAR to avoid skin stripping • May require primary contact layer • Poor absorption of highly viscous exudate	• Up to 4 days depending on personal choice
Keratin	• Keragel	• Chronic wounds	• Dilute with blend emollient if stinging occurs	• Reapply with dressing changes

- First choice of treatment when available: PolyMem, Flaminal Hydro/Forte
- Treatment of choice for chronic wounds based on consensus opinion per 2017 Best Practice Guidelines for skin and wound care in epidermolysis bullosa:

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
Polymeric membrane	• PolyMem • PolyMem Max • PolyMem WIC (under a secondary dressing or further layer of PolyMem)	• Infected wounds • Recalitrant wounds	• Can provide initial increase in exudate resulting in further skin damage if not properly controlled • Distinct smell does not necessarily indicate infection • Protect periwound skin	• Change when wet to avoid hypothermia

Dressing Type	Brand	Indications	Contraindication/ Comments	Wear Time
Enzyme alginogel	• Flaminal Hydro • Flaminal Forte	• Low exudate • High exudate	• Debrides, de-sloughs and antimicrobial • Has some action in modulating excess proteases • Can be used on all wounds apart from third degree burns • Do not use if patient has sensitivity to alginates or polyethylene glycol	• Re-apply at each dressing change at least 2mm thick
Honey		• Sensitive wounds	• Can cause transient stinging or pain due to its acidity and high osmotic 'pull' • In turn this will contribute to high levels of exudate	
Protease modulator	• UrgoTul Start range • Promogran • Promogran Prisma (with silver)	• When excess protease may be present	• Promogran/Promogran Prisma may cause initial transient stinging • Excess product cannot be saved once opened as it degrades on contact with air • A secondary dressing required and the product may provoke initial heavy exudate	• Frequent dressing changes may be required to avoid maceration

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RDEB	1 to 12 sheets topically to wound(s) per surgical session. Dose is based on surface area of wound. One sheet covers an area of 41.25 cm^2.	12 sheets/surgical session

VI. Product Availability

Sheet: 41.25 cm^2 (5.5 cm x 7.5 cm) affixed on a rectangular gauze and placed in a clear, thermoformed protective case containing sterile transport media sealed in packaging consisting of 4 levels of protection

VII. References

1. Zevaskyn Prescribing Information. Cleveland, OH: Abeona Therapeutics Inc; April 2025. Available at: https://d1io3yog0oux5.cloudfront.net/_97c62242a52d17e584a3147d26ed2790/abeonatherapeutics/files/ZEVASKYN_Final_Label_30Apr2025.pdf. Accessed May 13, 2025.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed May 13, 2025.
3. Denyer J, Pillay E, Clapham J. Best practice guidelines for skin and wound care in epidermolysis bullosa. An International Consensus. Wounds International, 2017.
4. Mariath LM, Santin JT, Schuler-Faccini L, Kiszewski AE. Inherited epidermolysis bullosa: update on the clinical and genetic aspects. An Bras Dermatol. 2020;95:551---69.
5. ClinicalTrials.gov. Phase 3, open-label clinical trial of EB-101 for the treatment of recessive dystrophic epidermolysis bullosa (RDEB). Available at: https://clinicaltrials.gov/ct2/show/NCT04227106. Accessed May 13, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3389	Topical administration, prademagene zamikeracel, per treatment

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	12.06.22	02.23
1Q 2024 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	11.20.23	2.24
1Q 2025 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	10.30.24	02.25
Drug is now FDA approved – criteria updated per FDA labeling; for initial therapy: for diagnosis of RDEB criteria, removed "immunofluorescence mapping, transmission electron microscopy, antigenic mapping" as EB diagnostic criteria is not specific to only RDEB and to align with Vyjuvek criteria; removed criteria "member has no evidence of immune response to COL7 as evidence by immunofluorescence (e.g., member is not positive for anti-COL7 antibodies at baseline)" as supported by prescribing information and specialist feedback; added requirement that Zevaskyn is not prescribed concurrently with Vyjuvek or Filsuvez; updated criteria from "wound sites must be stage 2 chronic wound" to "wound sites must be chronic open wounds (e.g., stage 2 chronic wound)"; revised maximum dosing from does not exceed 6 sheets to does not exceed 12 sheets per one-time surgical application; for	06.03.25	08.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Appendix E, removed supplemental diagnostic information on immunofluorescence mapping, transmission electron microscopy, antigenic mapping; for continued therapy, removed criteria "continued therapy will not be reauthorized as EB-101 is indicated to be a one-time surgical application" and added "Re-authorization is not permitted. Members must meet the initial approval criteria if request is for previously untreated or newly developed wounds"; references reviewed and updated.		
Updated language under Policy/Criteria to effectively redirect prior authorization reviews to Precision Drug Action Committee (PDAC) Utilization Management Review.	11.04.25	
Added Coding Implications section with HCPCS code [J3389].	01.06.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.